IN THE CLAIMS:

Please amend claims 169 and 187, cancel claims 188-198, and new claims 199-207.

This listing of claims will replace all prior versions, and listings of the claims in the application.

Listing of the claims

1-168. **(Canceled)**

169. **(Currently Amended)** A method of treating an individual who has metastasized colorectal cancer or primary or metastasized gastric or esophageal cancer in an individual who has been identified as having metastasized colorectal cancer or primary or metastasized gastric or esophageal cancer, said method comprising the steps in the following order:

a) administering to said individual a cytostatically effective amount of a guanylyl cyclase C ligand sufficient to inhibit cell proliferation by the cytostatic effect of the guanylyl cyclase C ligand for at least 6 hours wherein, wherein said guanylyl cycles C ligand activates guanylyl cyclase C on cancer cells, and <u>stimulates accumulation of intracellular cGMP, and</u>

b) subsequently after administration of said guanylyl cycles C ligand is completed administering a therapeutically effective amount of a cytotoxic therapeutic agent or radiation.

<u>wherein effectiveness of said therapeutically effective amount of a cytotoxic therapeutic agent or radiation is enhanced by prior inhibition of proliferation of cancer cells by said cytostatically effective amount of said guanylyl cyclase C ligand</u>.

170. **(Canceled)**

171. **(Previously presented)** The method of claim 169 wherein said cytotoxic therapeutic agent is selected from the group consisting of: methotrexate, doxorubicin, daunorubicin, cytosinarabinoside, etoposide, 5- fluorouracil, melphalan, chlorambucil, cis-

platin, vindesine, mitomycin, bleomycin, purothionin, macromomycin, 1,4 benzoquinone derivatives, trenimon, ricin, ricin A chain, Pseudomonas exotoxin, diphtheria toxin, Clostridium perfringens phospholipase C, bovine pancreatic ribonuclease, pokeweed antiviral protein, abrin, abrin A chain, cobra venom factor, gelonin, saporin, modeccin, viscumin, volkensin, nitroimidazole, metronidazole and misonidazole.

172. **(Previously presented)** The method of claim 169 wherein the individual has been identified as having metastatic colorectal, esophageal or stomach cancer.

173. **(Canceled)**

174. **(Previously presented)** The method of claim 169, wherein the cytostatically effective amount of a guanylyl cyclase C ligand is an amount sufficient to maintain a concentration of greater than or equal to 10 times the EC_{50} of said guanylyl cyclase C ligand.

175. **(Previously presented)** The method of claim 169 wherein said cytotoxic therapeutic agent is a guanylyl cyclase C ligand conjugated to a cytotoxic moiety.

176. **(Previously presented)** The method of claim 175 wherein said cytotoxic therapeutic agent is an anti-guanylyl cyclase C antibody conjugated to a cytotoxic moiety.

177. **(Previously presented)** The method of claim 169 wherein the guanylyl cyclase C ligand that activates guanylyl cyclase C on cancer cells is administered in an amount sufficient to inhibit cell proliferation by the cytostatic effect of the guanylyl cyclase C ligand for at least 8 hours.

178. **(Previously presented)** The method of claim 169 wherein the guanylyl cyclase C ligand that activates guanylyl cyclase C on cancer cells is administered in an amount sufficient

to inhibit cell proliferation by the cytostatic effect of the guanylyl cyclase C ligand for at least 12 hours.

179. **(Previously presented)** The method of claim 169 wherein the guanylyl cyclase C ligand that activates guanylyl cyclase C on cancer cells is administered in an amount sufficient to inhibit cell proliferation by the cytostatic effect of the guanylyl cyclase C ligand for at least 16 hours.

180. **(Previously presented)** The method of claim 169 wherein the guanylyl cyclase C ligand that activates guanylyl cyclase C on cancer cells is administered in an amount sufficient to inhibit cell proliferation by the cytostatic effect of the guanylyl cyclase C ligand for at least 20 hours.

181. **(Previously presented)** The method of claim 169 wherein the guanylyl cyclase C ligand that activates guanylyl cyclase C on cancer cells is administered in an amount sufficient to inhibit cell proliferation by the cytostatic effect of the guanylyl cyclase C ligand for at least 24 hours.

182. **(Previously presented)** The method of claim 169 wherein said guanylyl cyclase C ligand that activates guanylyl cyclase C on cancer cells is administered intravenously.

183. **(Previously presented)** The method of claim 169 wherein said guanylyl cyclase C ligand that activates guanylyl cyclase C is administered for 7-15 days followed by treatment using said cytotoxic agent.

184. **(Previously presented)** The method of claim 169 wherein said guanylyl cyclase C ligand that activates guanylyl cyclase C is administered for 30 days followed by treatment using said cytotoxic agent.

185. **(Previously presented)** The method of claim 169 comprising administering more than one cytotoxic agent

186. **(Previously presented)** The method of claim 169 comprising administering one cytotoxic agent that selectively kills cells in S phase and one cytotoxic drug that selectively kills cells in G1 phase.

187. **(Currently amended)** The method of claim 169 wherein said cytotoxic therapeutic agent is selected from the group consisting of: methotrexate, doxorubicin, daunorubicin, cytosinarabinoside, etoposide, 5- fluorouracil, melphalan, chlorambucil, cis-platin, vindesine, mitomycin, bleomycin, purothionin, macromomycin, 1,4 benzoquinone derivatives, ~~,~~-nitroimidazole, metronidazole and misonidazole.

188-198. **(Canceled)**

199. **(New)** A method of treating an individual who has metastasized colorectal cancer or primary or metastasized gastric or esophageal cancer in an individual who has been identified as having metastasized colorectal cancer or primary or metastasized gastric or esophageal cancer, said method comprising the steps in the following order:

a) administering to said individual for a period sufficient to inhibit the proliferation of cancer cells, a cytostatically effective amount of a guanylyl cyclase C ligand that activate guanylyl cyclase C on cancer cells, wherein said activation of guanylyl cyclase C stimulates intracellular accumulation of cGMP and inhibits proliferation of said cancer cells; and

b) subsequently after administration of said guanylyl cyclase C ligand is completed administering a therapeutically effective amount of a cytotoxic therapeutic agent or radiation;

wherein effectiveness of said therapeutically effective amount of a cytotoxic therapeutic agent or radiation is enhanced by prior inhibition of proliferation of cancer cells by said cytostatically effective amount of said guanylyl cyclase C ligand.

200. **(New)** The method of claim 199 wherein said cytotoxic therapeutic agent is selected from the group consisting of: methotrexate, doxorubicin, daunorubicin, cytosinarabinoside, etoposide, 5- fluorouracil, melphalan, chlorambucil, cis-platin, vindesine, mitomycin, bleomycin, purothionin, macromomycin, 1,4 benzoquinone derivatives, trenimon, ricin, ricin A chain, Pseudomonas exotoxin, diphtheria toxin, Clostridium perfringens phospholipase C, bovine pancreatic ribonuclease, pokeweed antiviral protein, abrin, abrin A chain, cobra venom factor, gelonin, saporin, modeccin, viscumin, volkensin, nitroimidazole, metronidazole and misonidazole.

201. **(New)** The method of claim 199 wherein the individual has been identified as having metastatic colorectal, esophageal or stomach cancer.

202. **(New)** The method of claim 199 wherein said cytotoxic therapeutic agent is a guanylyl cyclase C ligand conjugated to a cytotoxic moiety.

203. **(New)** The method of claim 199 wherein said cytotoxic therapeutic agent is an anti-guanylyl cyclase C antibody conjugated to a cytotoxic moiety.

204. **(New)** The method of claim 199 wherein said guanylyl cyclase C ligand that activates guanylyl cyclase C on cancer cells is administered intravenously.

205. **(New)** The method of claim 199 comprising administering more than one cytotoxic agent

206. **(New)** The method of claim 199 comprising administering one cytotoxic agent that selectively kills cells in S phase and one cytotoxic drug that selectively kills cells in G1 phase.

207. **(New)** The method of claim 199 wherein said cytotoxic therapeutic agent is selected from the group consisting of: methotrexate, doxorubicin, daunorubicin, cytosinarabinoside, etoposide, 5- fluorouracil, melphalan, chlorambucil, cis-platin, vindesine, mitomycin, bleomycin, purothionin, macromomycin, 1,4 benzoquinone derivatives, , nitroimidazole, metronidazole and misonidazole.